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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/402,277	09/30/99	KAWASHIMA E	018428-00030

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EXAMINER	
LU,F	
ART UNIT	**PAPER NUMBER**
1655	8

DATE MAILED: 07/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

US GPO 2000; 465-188/25266

Office Action Summary

Application No.	Applicant(s)
09/402,277	Kawashima et al.,
Examiner	**Group Art Unit**
Frank Lu	1655

☒ Responsive to communication(s) filed on *Sep 30, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-30 and 59-65* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-26 and 59-64* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-30 and 59-65* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Location of Application

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1655.

Election/Restriction

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CAR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-26 and 59-64, drawn to a method of nucleic acid amplification (claims 1-26) and apparatus for performing above method (claims 59-64).

II. Claims 27-30 and 65, drawn to a plurality of immobilized nucleic acid (claims 27-30) and a kit for use in screening, diagnosis or in nucleic acid sequencing (claim 65).

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different process of using that product such as a hybridization assay.

During a telephone conversation with Mr. William Smith (Registration No: 30,223) on May 15, 2000 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-26 and 59-64. Affirmation of this election must be made by applicant in replying to this Office action. Claims 27-30 and 65 have been withdrawn from further consideration by the examiner, 37 CAR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CAR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CAR 1.48(b) and by the fee required under 37 CAR 1.17(i).

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CAR 1.78). This examiner suggests that applicants insert all documents, e.g.GB 9713238.5, which have been claimed foreign priority by applicants, into the first sentence of the specification.

Drawings

4. The drawings are objected to for reasons as stated on FORM PTO-948 (Rev. 8-98). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Sequence Rules Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CAR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CAR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Direct the reply to the undersigned.

Specification

6. The disclosure is objected to because of the following informalities: (1) at pages 18 and 19 of specification there is provided description for each of Figures 1 to Figure 19. Upon reviewing the figures, however, there are found Figures 1-1 and 1-2, Figures 4a and 4b, Figures 5-1 and 5-2, Figures 6(a) and 6(b), Figures 7-1 and 7-2, Figures 8-1 and 8-2, and Figures 10-1 to 10-3, Figures 11-1 and 11- 2, Figures 12-1 and 12-2, and Figures 2A and 2B. Each figure, e.g. 1A, is considered to be a separate figure and needs to be described in the specification; (2) at page 19, the examiner notices that Figures 18 and 19 were described together. Since Figures 18 and 19 are considered to be a separate figure, a separate description is needed in the specification; (3) Figure number on line 5 of page 68 is wrong since there is no Figure 21 in this application.

Please check the specification for mistakes. Appropriate correction is required.

Claim Objections

7. Claim 1 is objected to because of the following informalities: no period should appear after the label of each step, e.g., "a." should be --a)--.

8. Claim 17 is objected to because of the following informalities: missing a "or" between the coma and "is" on line 2 of the claim.

9. Claims 62-64 are objected to because of the following informalities: (1) claims 62 and 63 are dependent on claim 61 which is based on non-elected claim 27; (2) claim 64 is dependent on claim 63.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 3-6, 11, 12, 19-21, 61, and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 3-6 are rejected as vague and indefinite over the phrase "wherein said single-stranded target nucleic acid is produced by providing a given nucleic acid sequence to be amplified" in claims 3 and 4 because it is unclear what "wherein said single-stranded target nucleic acid is providing a given nucleic acid sequence to be amplified" means here. For example, does "a given nucleic acid sequence " mean an immobilized primer or does "a given nucleic acid sequence" mean a product amplified from an immobilized primer? Note that this rejection also includes claims 5 and 6 which are dependent on claim 3. This rejection can be rejected by clarifying the meaning of "wherein said single-stranded target nucleic acid is produced by providing a given nucleic acid sequence to be amplified" in claims 3 and 4.

12. Claim 5 is rejected as vague and indefinite over the phrase "at first and second ends of said single-stranded target nucleic acid" because it is unclear what "at first and second ends of said single-stranded target nucleic acid" means here. For example, does "first and second ends" mean 5' and 3' ends of said single-stranded target nucleic acid or does "first and second ends" mean

something else? This rejection can be rejected by clarifying the meaning of "at first and second ends of said single-stranded target nucleic acid" in the claim.

13. Claim 19-21 are rejected as vague and indefinite over the word "part" on line 3 of claims 19 and 21 because it is unclear what "part" means here. For example, how large "part" is in nucleic acid molecule? Does "part" mean one nucleotide or does " part" mean something else?. This rejection can be rejected by clarifying the meaning of "part" in claims 19 and 21.

14. Claim 62 is rejected as vague and indefinite over the phrase "so that another nucleic acid strand is located on the surface within a distance of the length of that strand " because it is unclear what "that strand" means here. For example, does "that strand " mean identical nucleic acid strand or does "that strand " mean identical complementary strand? This rejection can be rejected by clarifying the meaning of "that strand " in the phrase "so that another nucleic acid strand is located on the surface within a distance of the length of that strand "

15. The term "substantially " in claims 11 and 12 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

16. Claims 61 recites the limitation "claim 27" in the claims. There is insufficient antecedent basis for this limitation in the claim because claim 27 is non-elected.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-26 and 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hosoi *et al.*, (European Patent No: 665293 A2, published on February 8, 1995) in view of Cheng *et al.*, (Nucleic Acids Res. 24, 380-395, January 1996) and Hahn *et al.*, (Anal Biochem. 229, 236-248, August 1995).

Hosoi *et al.* teach: (1) hybridizing each of plural primers comprising oligonucleotide with a template comprising a single-stranded nucleic acid to be examined, thereby to form complex having a double-stranded portion comprising a portion of the template and the primer, the plural primers being separately disposed in a plurality of regions in accordance with the kinds of the primers; (2) substantially simultaneously adding plural kinds of nucleotides or nucleotide

analogues to the complexes respectively disposed in the plural regions, thereby to perform growth reaction of the primer with the nucleic acid to be examined as the template in a direction of from 5' to 3' of the primer, the plural kinds of nucleotides or nucleotide analogues being complementary to nucleotides constituting the template in the complex, and being capable of forming base pair with nucleotides constituting the template; (3) detecting the amount of the growth of the primers (abstract); (4) a plurality of oligonucleotides including all of the combinations comprising k bases as plural primers were fixed into plural columns in a capillary plate (AC) with a square shape (Figure 1); (5) four different fluorescent-dNTP as tags; (6) a detection apparatus comprising a charge coupled device (page 14, second paragraph and a magnify device (page 16, third paragraph, method step (III)). More specifically, trimers (3 mers) of all of the combinations containing A, T, G, and C, were fixed into 64 columns of the glass capillary plate, as shown in Figure 8 (page 13, fifth paragraph). The primer disposed in each column was hybridized with the nucleic acid to be examined. The nucleic acid to be examined which has not been hybridized with the primer was washed out (page 13, sixth paragraph); Then four kind of fluorescent-dNTPs were simultaneously added together with DNA polymerase, a unidirectional extension reaction of each of the primers occurred in the direction corresponding to the direction of from 5' to 3' of the primer (see Figure 9B) (page 13, seventh paragraph). After the reaction, the resultant capillary plate CA was placed in a dark DB box as shown in Figure 10A, which constitutes an apparatus for determining the base sequencing of nucleic acid. The apparatus as shown in Figure 10A comprises: the dark box DB1 for housing the capillary plate CA so as to shut off external light; an excitation light source 70 (such as Xenon lamp) for supplying excitation light to the capillary plate

CA; and a CCD television camera 10 disposed on a surface on side of the dark box DB1, for picking up an image of the capillary plate CA (page 14, second paragraph). Note that sequencing reactions were performed by incubating the above test tube at 95^0 C (30 seconds), at 41^0 C (30 seconds), and at 72^0 C (5 minutes) (page 15).

Hosoi *et al.* do not disclose PCR on the solid support and restriction enzyme digestion.

Cheng *et al.* teach performing PCR in microfabricated silicon-glass chips using Taq DNA polymerase. The general PCR priniciple from this paper clearly read the steps (C) to (E) of claim 1, claims 2, 15, 16, 22, and 60. Specifically, they examined PCR in silicon dioxide-coated silicon-glass chips (12 µl in volume with a surface to volume ratio of approximately 17.5 $mm^2/\mu l$) using two PCR reagent systems: (1) the conventional reagent system using Taq DNA polymerase; (ii) the hot-start reagent system based on a mixture of TaqStart antibody and Taq DNA polymerase. Quantitative results obtained from capillary electrophoresis for the expected amplification products showed that amplification in microchips was reproducible (between batch coefficient of variation 7.71%) and provided excellent yields. They also used the chip for PCR directly from isolated intact human lymphocytes. The amplification results were comparable with those obtained using extracted human genomic DNA (page 380, abstract).

Cheng *et al.*, do not disclose to preform PCR using a plurality of primers, restriction enzyme digestion and a detection method.

Hahn *et al.*, teach quantitative polymerase chain reaction with enzyme-linked immunosorbent assay detection of selectively amplified sample and control DNA digested restriction enzyme (see abstract in page 236).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have performed PCR on the solid support immobilized with a plurality of identical or different primers using single stranded nucleic acid templates and fluorescent-dNTPs as suggested by Cheng *et al.* and detected signals from PCR products using apparatus comprising a CCD camera and a magnifying device. The prior arts provided by Hosoi *et al.* and Hahn *et al.* would have motivated one having ordinary skill in the art to perform PCR on the solid support such as a capillary plate immobilized with a plurality of identical or different primers using single stranded nucleic acid templates and fluorescent-dNTPs, cleave PCR products by a specific restriction enzyme and further detected signals using apparatus comprising a CCD camera and a magnifying device because the sequencing apparatus with temperature range (41 °C-95 °C) has suggested its application in PCR. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these methods together because all of these methods are known in the art and are easy to use.

Conclusion

19. No Claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94

(December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
July 14, 2000

B. L. Sisson
BRADLEY L. SISSON
PRIMARY EXAMINER
GROUP 1800 1650
7/17/00

Application No. 09/402,277

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 CFR 1.821-1.825. Applicant's attention is directed to these regulations, published at 114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).

☐ 7. Other: _____

Applicant must provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact

For Rules Interpretation, call (703) 308-1123
For CRF submission help, call (703) 308-4212
For PatentIn software help, call (703) 557-0400

Please return a copy of this notice with your response.